3-16-07

Ffw

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service as Express Mail, Label No. EV 756034636 USus, on the date shown below in an envelope addressed to: MS Amendment, Commissioner for Patents, BO. Box 1450, Alexandria, VA 22313-1450.

Qated: March 14, 2007

Signature: (Peter C. Lauro)

Docket No.: 65350US(54086)

(PATENT)

MAR 1 4 2007

OIP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Patent Application of:

Chael V. Agrez

Application No.: 10/575,736

Filed: April 13, 2006

For: METHODS AND AGENTS FOR THE

TREATMENT OF CANCER

Confirmation No.: 9415

Art Unit: N/A

**Examiner: Not Yet Assigned** 

## SUPPLEMETAL INFORMATION DISCLOSURE STATEMENT (SIDS)

MS Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. §§1.56, 1.97 and 1.98, Applicant invites the attention of the Patent and Trademark Office to the references listed on the attached PTO/SB/08. Applicant respectfully requests that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Supplemental Information Disclosure Statement is filed more than three months after the date of entry of the national stage of the corresponding PCT application, BUT before the mailing date of the first Office Action on the merits. (37 C.F.R. §1.97(c)).

In accordance with 37 C.F.R. §1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents and U.S. patent applications. Applicant submits herewith copies of foreign patents and non-patent literature in accordance with 37 C.F.R. §1.98(a)(2).

Applicant notes that references BD, CF and CE2 were cited in a Search Report issued during prosecution of GB patent No. 2409679, which issued from GB application

Application No.: 10/575,736 Docket No.: 65350US(54086)

**Supplemental Information Disclosure Statement** 

No. 422989.4, which corresponds to the instant application. A copy of the GB Search Report (ref. BI) is enclosed for the Examiner's convenience. The remaining references cited on the GB Search Report were made of record in the Information Disclosure Statement filed on April 13, 2006.

In accordance with 37 C.F.R. §1.97(g), the filing of this Supplemental Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 C.F.R. §1.56(a) exists. In accordance with 37 C.F.R. §1.97(h), the filing of this Supplemental Information Disclosure Statement shall not be construed to be an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

Applicant submits that the Supplemental Information Disclosure Statement is in compliance with 37 C.F.R. §1.98 and respectfully requests that the Examiner consider and make of record the listed references.

Applicant believes that no fees are required for consideration and entry of this Supplemental Information Disclosure Statement. Nevertheless, the Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 65350US(54086). A duplicate copy of this paper is enclosed.

Dated: March 14, 2007

Peter C. Lauro, Esq.

Respectfully submitted

Registration No.: 32,360

**EDWARDS ANGELL PALMER & DODGE LLP** 

P.O. Box 55874

Boston, Massachusetts 02205

(617) 439-4444

Attorneys/Agents For Applicant

Application No. (if known): 10/575,736

Attorney Docket No.: 65350US(54086)

## **Certificate of Express Mailing Under 37 CFR 1.10**

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail, Airbill No. EV 756034636 USus in an envelope addressed to:

MS Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

on	•
Date	_
( ) let	CLauro
	Signature
F	Peter C. Lauro, Esq.
Typed or printed	name of person signing Certificate
32,360	(617) 439-4444
Registration Number, if applicable	Telephone Number
•	

Note: Each paper must have its own certificate of mailing, or this certificate must identify each submitted paper.

Supplemental Information Disclosure Statement (2 pages)
Citation (PTO/SB/08/A/B) by Applicant (115 References and GB Search
Report) (6 pages)
Copies of 99 References and GB Search Report

PTO/SB/08A/B (09-06)

Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Substitu	Substitute for form 1449/PTO			Complete if Known		
٠				Application Number	10/575,736	
INF	<b>ORMATIC</b>	ON DI	SCLOSURE	Filing Date	April 13, 2006	
STA	STATEMENT BY APPLICANT			First Named Inventor	Michael V. Agrez	
				Art Unit	N/A	
	(Use as many sheets as necessary)			Examiner Name	Not Yet Assigned	
Sheet	1	of	6	Attorney Docket Number	65350US(54086)	

		-	U.S. PA	TENT DOCUMENTS	
Examiner	Cite	Document Number	Publication Date	Name of Patentee or	Pages, Columns, Lines, Where Relevant Passages or Relevant
Initials*	No.1	Number-Kind Code <sup>2</sup> ( if known)	MM-DD-YYYY	Applicant of Cited Document	Figures Appear
	AA*	US-5,593,884	01-14-1997	Karin et al.	
	AB*	US-2004/0147435		Hawiger et al.	
	AC*	US-5,807,746	09-15-1998	Lin et al.	
	AD*	US-5,962,643	10-05-1999	Sheppard et al.	
	AE*	US-6,007,991	12-28-1999	Sivaraman et al.	
	AF*	US-6,043,339	03-28-2000	Lin et al.	
	AG*	US-6,248,558	06-19-2001	Lin et al.	
	AH*	US-6,312,956	11-06-2001	Lane	
	AI*	US-6,339,148	01-15-2002	Sheppard et al.	
	AJ*	US-6,432,680	08-13-2002	Lin et al.	
	AK*	US-6,495,518	12-17-2002	Hawiger et al.	
	AL*	US-6,576,432	06-10-2003	Sheppard et al.	
	AM*	US-6,596,277	07-22-2003	Sheppard et al.	
	AN*	US-6,639,056-A1	10-28-2003	Sheppard et al.	
	AO*	US-6,780,843-A1	08-24-2004	Lin et al.	
	AP*	US-6,787,322-A1	09-07-2004	Sheppard et al.	

		FOREIG	ON PATENT	DOCUMENTS		
Examiner Initials*	Cite No.1	Foreign Patent Document  Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T⁵
	ВА	WO 91/19008		BOULTON		
	ВВ	WO 92/12236		SHEPPARD		
	ВС	WO 95/34295		LIN		
	BD	WO 98/16241		VANDERBILT UNIVERSITY		
	BE	WO 99/09214		MCKAY		
	BF	WO 99/49879		LIN		
	BG	WO 00/59549		MCKAY		
	ВН	WO 01/37821		HAWIGER		
	BI	GB Search Report	-			

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. \*CITE NO.: Those application(s) which are marked with an single asterisk (\*) next to the Cite No. are not supplied (under 37 CFR 1.98(a)(2)(iii)) because that application was filed after June 30, 2003 or is available in the IFW. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at <a href="www.uspto.gov">www.uspto.gov</a> or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

NON PATENT LITERATURE DOCUMENTS							
Examiner	Examiner Cite No.1 Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, iournal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city T2						
Examiner   Date   Considered							

597009

Sub	ostitute for form 1449/PTO			Complete if Known		
				Application Number	10/575,736	
11	<b>NFORMATION</b>	l Di	SCLOSURE	Filing Date	April 13, 2006	
l s	TATEMENT E	3Y /	APPLICANT	First Named Inventor	Michael V. Agrez	
				Art Unit	N/A	
	(Use as many sheets as necessary)			Examiner Name	Not Yet Assigned	
Sheet	Sheet 2 of 6		Attorney Docket Number	65350US(54086)		

Initials		and/or country where published.	
	CA	Agrez, M., et al., "The $\alpha_v\beta_0$ integrin promotes proliferation of colon carcinoma cells through a unique region of the $\beta_0$ cytoplasmic domain". J. Cell. Biol. 127, No. 2, pp.547-556 (1994).	
	СВ	Agrez, M.V., "Cell adhesion molecules and colon cancer", A.N.Z.J. Surgery 66, 789-796 (1996).	
	СС	Agrez, et al., "The avβ6 integrin induces gelatinase B secretion in colon cancer cells", Int. J. Cancer 81 (1), 90-7 (1999).	
	CD	Agrez, M.V. et al., "Colorectal cancer and the integrin family of cell adhesion receptors: current status and future directions", European Journal of Cancer 30A, 2166-2170 (1994).	
	CE	Agrez, M.V. et al., "Multiplicity of fibronectin-binding a v integrin receptors in colorectal cancer", Br. J. Cancer 73, 887-892 (1996).	
	CF	Ahmed, N. et al., "Direct integrin $\alpha_{\nu}\beta_{6}$ - ERK binding: implications for tumour growth". Oncogene 21, 1370-1380 (2002).	
	CG	Bookstein, R. et al, "p53 gene therapy <i>in vivo</i> for hepatocellular and liver metastatic colorectal cancer", Seminars Oncol. 23, 66-77 (1996).	
	СН	Boudreau, N.J and Jones, P.L., "Extracellular matrix and integrin signalling: the shape of things to come". Brochem, J. 339, 481-488 (1999).	
	CI	Boulton, T.G., et al., "ERKs: a family of protein-serine/threonine kinases that are activated and tyrosine phosphorylated in response to insulin and NGF", Cell 65, 663-675 (1991).	
	CJ	Boulton, T.G., et al., "Mitogen-activated protein kinase 1," (EC 2.7.1) (1991) (Swiss Prot Acc No. P27703).	
	СК	Bruess, J.M., et al., "The integrin a 6 $\beta$ 1, is necessary for the matrix-dependent activation of FAK and MAP Kinase and the migration of human hepatocarcinoma cells," Hepatology, Jul 34(1), 42-9 (2001).	
	CL	Carlone, V. et al., "The Integrin, $a_6\beta_1$ , is necessary for the matrix-dependent activation of FAK and MAP kinase and the migration of human hepatocarcinoma cells. Hepatology. Vol. 34, No. 1, 42-49 (2001).	
	СМ	Chen et al,. "Distinct structural requirements for interaction of the integrins a5β1, avβ5, and avβ6 with central cell binding domain in fibronectin," Cell Adhesion and Communication, Vol. 4, Nos. 4-5, pp 237-250 (1996).	
	CN	Cone et al., "Effects of $\beta$ subunit cytoplasmic domain deletions on the recruitment of the integrin av $\beta$ 6 to focal contact", Cell Adhesion and Communication, Vol. 2, pp. 101-113 (1994).	
	СО	Coppolino et al., "Bi-directional signal transduction by integrin receptors," The International Journal of Biochemistry & Cell Biology, Vol. 32, pp 171-188 (2000).	
	СР	Coppolino, M. et al., "Inducible interaction of integrin alpha 2 beta 1 with calreticulin.  Dependence of the activation state of the integrin", J. Biol. Chem. 270, 23132-23138 (1995).	
	CQ	Dedhar, S. and Hannigan, G.E., "Integrin cytoplasmic interactions and bidirectional transmembrane signalling". Curr. Op. Cell Biol. Vol. 8, No. 5, 657-669 (1996)	
	CR	Dixit et al., "Identification of a sequence within the integrin $\beta$ 6 subunit cytoplasmic domain that is required to support the specific effect of av $\beta$ 6 on proliferation in three-dimensional culture", J Biol. Chem., Vol 271, No. 42, pp 25976-25980 (1996).	
	CS	Eliceiri, B.P., et al., "The role of av integrins during angiogenesis: insights into potential mechanisms of action and clinical development," J Clin Invest (1999), 103(9), 1227-30.	
	СТ	Eliceiri. B.P., et al., "Integrin av83 requirement for sustained mitogen activated protein kinase	

Examiner	Date
Signature	Considered
507000	

Complete if Known Substitute for form 1449/PTO 10/575,736 Application Number **INFORMATION DISCLOSURE** April 13, 2006 Filing Date STATEMENT BY APPLICANT First Named Inventor Michael V. Agrez **Art Unit** N/A (Use as many sheets as necessary) Not Yet Assigned Examiner Name 3 6 65350US(54086) Sheet of Attorney Docket Number

	CO1	Ishii. T., et al., "Integrin-linked kinase controls neurite outgrowth in N1E-115 neuroblastoma  Date
	CN1	Hughes, P.E. and Pfaff, M., "Integrin affinity modulation". Trends. Cell Biol. Vol. 8, No. 9, 359-364 (1998)
<u> </u>	CM1	Howe, A. et al., "Integrin signaling and cell growth control", Curr. Opin. Biol. 10, 220-231 (1998).
	CL1	Horwitz, A. et al., "Interaction of plasma membrane fibronectin receptor with a talin-a transmembrane linkage", Nature 320, 531-533 (1986).
		monoclonal antibodies against the beta 1 integin subunit during wound healing in organ culture", Invest. Opthalmol. Vis. Sci. 34, 2761-2768 (1993).
	CK1	Hergott, G.J. et al., "Inhibition of retinal pigment epithelial cell migration and proliferation with
	CJ1	Hemler, M.E., "Integrin associated proteins", Curr. Opin. Biol. 10, 578-585 (1998).
	CI1	beta 1-integrin-linked protein kinase", Nature 379, 91-96 (1996).  von Heijne, G., "The Signal Peptide". Topical Review. J. Membrane Biol. 115, 195-201 (1990)
	CG1 CH1	Gupta, K., et al., "VEGF prevents apoptosis of human microvascular endothelial cells via opposing effects on MAPK/ERK and SAPK/JNK signaling," Exp Cell Res (1999), 247(2): 495-504.  Hannigan, G.E. et al., "Regulation of cell adhesion and anchorage-dependent growth by a new
	CF1	Guan, J.L. et al., "Regulation of focal adhesions-associated protein tyrosine kinase by both cellular adhesion and oncogenic transformation", Nature 358, 690-692 (1992).
	CE1	Gu, J. et al., "Tumor suppressor PTEN inhibits integrin - and growth factor - mediated nitrogen activated protein (MAP) kinase signalling pathways". J. Cell Biol. Vol. 143, No. 5, 1375-1383 (1998)
	CD1	Grammer, T.C. et al., "Evidence for MEK-independent pathways regulating the prolonged activation of the ERK-MAP kinases", Oncogene 14, 1635-1642 (1997).
	CC1	Gotoh et al., "Cross-Linking of Integrins Induces Tyrosine Phosphorylation of the Proto- Oncogene Product Vav and the Protein Tyrosine Kinase Syk in Human Factor-dependent Myeloid Cells", Cell Growth and Differentiation, Vol. 8, pp. 721-729 (1997).
	CB1	Gorziglia, M. and Kapikian, A.Z., "Expression of the OSU rotaravirus outer capsid protein VP4 by an adenovirus recombinant". J. Virol., pp 4407-4412, July (1992)
	CA1	Gonzalez, F.A., "H Sapiens 40kDa protein kinase related to rat ERK2," (1992) (GenPept Acc No. CAA77753).
	CZ	Giancotti, F.G. et al., "Integrin signaling", Science 285, 1028-1032 (1999). Gorgziglia and Kapikian, J., Virol. 66, 4407-4412 (1992).
	CY	Garrington, T.P. et al., "Organization and regulation of mitogen-activated protein kinase signaling pathways", Curl. Opin. Biol. 11, 211-218 (1999).
	CX	Gamble, J. R. et al., "Regulation of <i>in vitro</i> capillary tube formation by anti-integrin antibodies", J. Cell Biol. 121, 931-943 (1993).
	CW	Friedlander, M., et al., "Definition of two angiogenic pathways by distinct a v integrins," Science (1995), 270(5241): 1500-2.
	CV	Fodstad, O. et al., Database Geneseq 'Online', "CAPL gene 5' splice site antisense oligonucleotide", Database Accession No. AAT33333 (12 November 1996)
	CU	Erker, J.C. et al., Database GenBank 'Online', "Polyprotein GB virus c/Hepatitis C virus", Database Accession No. AAC55951 (13 November 1996) (Abstract)
		activity during angiogenesis," J Cell Biol (1998), 140(5): 1255-63.

Considered

PTO/SB/08A/B (09-06)

Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number. Complete if Known Substitute for form 1449/PTO Application Number 10/575,736 **INFORMATION DISCLOSURE** April 13, 2006 Filing Date STATEMENT BY APPLICANT First Named Inventor Michael V. Agrez Art Unit N/A (Use as many sheets as necessary) Examiner Name Not Yet Assigned 4 6 65350US(54086) Sheet Attorney Docket Number

 1		
	cells," J. Biol. Chem. 276(46): 42994-43003 (2001).	
CP1	Johnson O.L. and Tracey, M.A., Encyclopaedia of Controlled Drug Delivery. Vol. 2, pp. 816-833. Edith Mathiowitz, John Wiley & Sons, Inc. New York (1999)	
 CQ1	Kerr, et al., "Novel small a v integrin antagonists: Comparative anti-cancer efficacy with known angiogenesis inhibitors", Anticancer Res 19 (2A), 959-68, (1999).	
 CR1	Knezevic, I. et al., "Direct binding of the platelet integrin alpha lib beta 3 (Pella) to talin. Evidence that interaction is mediated through the cytoplasmic domains of both alpha llb and beta 3", J. Biol. Chem. 271, 16416-16421 (1996).	
 CS1	Komberg, L. et al., "Cell adhesion or integrin clustering increases phophorylation of a focal adhesion-associated tyrosine kinase", J. Biol. Chem. 267, 23439-23442 (1992).	
CT1	Lin et al., "Integrin-mediated Activation of MAP Kinase Is Independent of FAK: Evidence for Dual Integrin Signaling Pathways in Fibroblasts", J. Cell. Biol., Vol. 136, No. 6, (1997)	
CU1	Lin, Y-Z et al., "Inhibition of nuclear translocation of transcription factors NF-kB by a synthetic peptide containing a cell membrane-permeable motif and nuclear localization sequence". J. Biol. Chem. Vol. 230, No. 24, 14255-14258 (1995)	
CV1	Liu, S., et al., "Binding of paxillin to $a_4$ integrins modifies integrin-dependent biological responses". Nature. Vol. 402, 666-681 (1999).	
CW1	Liu, X-Y, et al., "Identification of a functionally important sequence in the cytoplasmic tail of integrin $\beta_3$ by using cell-permeable peptide analogs". Proc. Natl. Acad. Sci. USA. Vol. 93, 11819-11824 (1996)	
CX1	Loftus, J.C et al., "Integrin-mediated cell adhesion: the extracellular face", J. Biol. Chem. 269, 25235-25238 (1994).	
CY1	Lub, M., et al; "Cytoplasmic tails of $\beta_1$ , $\beta_2$ , and $\beta_7$ integrins differentially regulate LFA-1 function in K562 cells". Mol. Biol. Cell, Vol. 8, 719-728 (1997)	
 CZ1	Maniero, F., et al., "The coupling of $a_6\beta_4$ integrin to Ras-MAP kinase pathways mediated by Shc controls keratinocyte proliferation". EMBO J. Vol. 16, No. 9, 2365-2375 (1997)	
CA2	Marcantonio, E.E., et al., "Mapping of the functional determinants of the integrin $\beta_1$ cytoplasmic domain by site-directed mutagenesis". Cell Reg. Vol. 1, 591-604 (1990)	
CB2	Mastrengelo, A.M., et al., "Amino acid motifs required for isolated $\beta$ cytoplasmic domains to regulate 'in trans' $\beta_1$ integrin conformation and function in cell attachment". J. Cell. Science, 112, 217-229 (1999)	
CC2	Meurers, B.H. et al., Database GenBank 'Online'. "Myosin heavy chain 12 'Homo Sapiens'", Database Accession No. CAA69036 (8 January 1997) (Abstract)	
CD2	Miranti, C.K. et al., "Protein Kinase C regulates integrin-induced activation of the extracellular regulated kinase pathway upstream of Shc", J. Biol. Chem. 274, 10571-10581 (1999).	
CE2	Niu, J., et al., "Integrin expression in colon cancer cells is regulated by the cytoplasmic domain of the $\beta_6$ integrin submit". Int. J. Cancer. 99, 529-537 (2002)	
CF2	Oda, K. et al., Database GenBank 'Online', "CoxII intron2 ORF 'Marchantia polymorpha!", Database Accession No. AAC09431 (2 April 1998) (Abstract)	
CG2	Otey, C.A. et al., "An interaction between alpha-actinin and beta 1 integrin subunit in vitro", J. Cell Biol. 111, 721-729 (1990).	
CH2	O'Toole, T.E., et al., "Regulation of integrin affinity states through an NPXY motif in the $\beta$ subunit cytoplasmic domain". J. Biol. Chem. Vol. 270, No. 15, 8553-8558 (1995)	
 CI2	Pagès. G., et al., "Signaling angiogenesis via p42/p44 MAP kinase cascade." Ann NY Acad	

Examiner	Date	*
Signature	Considered	
E07000		

Substitu	ute for form 1449/P	 ΤΟ			Complete if Known
				Application Number	10/575,736
INF	ORMATI	ON DIS	SCLOSURE	Filing Date	April 13, 2006
ST	STATEMENT BY APPLICANT			First Named Inventor	Michael V. Agrez
İ				Art Unit	N/A
	(Use as man	y sheets as i	necessary)	Examiner Name	Not Yet Assigned
Sheet	5	of	6	Attorney Docket Number	65350US(54086)

-	Sci, 902: 187-200, (2000).	
CJ2	Pardi, R., et al., "Conserved regions in the cytoplasmic domains of the leukocyte integrin $a_1\beta_2$ are involved in endoplasmic reticulum retention, dimerization, and cytoskeletal association". J. Immunol. Vol. 155, No. 3, 1252-1263 (1995)	
CK2	Patil, S., et al., "A double mutation of the NPLY motif in the integrin $\beta$ 3 cytoplasmic tail abolishes post-ligand binding events of $\beta$ 3 integrins". Vol. 7, No. Suppl. p.248A (1996) (Abstract)	
CL2	Payne, D.M. et al., "Identification of the regulatory phosphorylation sites in pp42/mitogen-activated protein kinase (MAP kinase)", EMBOJ 10, 885-892 (1991).	
CM2	Pfaff, M. et al., "Integrin beta cytoplasmic domains differentially bind to cytoskeletal proteins", J. Biol. Chem. 273, 6104-6109 (1998).	
CN2	Pillinger, M., et al., "Modes of action of aspirin-like drugs: Salicylates inhibit Erk activation and integrin-dependent neutrophil adhesion". Proc. Natl. Acad. Sci. USA. Vol. 95, 14540-14545 (1998)	. 1 FFT
CO2	Redlitz, A., et al., "Angiostatin diminishes activation of the mitogen-activated protein kinases ERK-1 and ERK-2 in human dermal microvascular endothelial cells." J Vasc Res, 36(1): 28-34, (1999).	
CP2	Reszka, A.A. et al., "Identification of amino acid dequences in the integrin beta 1 cytoplasmic domain implicated in cytoskeletal association", J. Cell Biol. 117, 1321-1330 (1992).	
CQ2		
CR2	Rojiani, M.V. et al., "In vitro interaction of a polypeptide homologous to human Ro/SS-A antigen (calreticulin) with a highly conserved amino acid sequence in the cytoplasmic domain of integrin alpha subunits", Biochemistry 30, 9859-9866 (1991).	
CS2	Schaller, M.D. et al., "Focal adhesion kinase and paxillin bind to peptides mimicking beta integrin cytoplasmic domains", J. Cell Biol. 130, 1181-1187 (1995).	
CT2	Sebolt-Leopold, J.S., et al., "Blockade of the MAP kinase pathway suppresses growth of colon tumors in vivo". Nature Medicine. Vol. 5, No. 7, 810-816 (1999)	
CU2	Sheppard, D. et al., "Complete amino acid sequence of a novel integrin $\beta$ subunit ( $\beta$ 6) identified in epithelial cells using the polymerase chain reaction", J. Biol. Chem. 265, 11502-11507 (1990).	
CV2	Sugiura, N., et al., "Mus muculus DNA for ERK2," exon 7. (GenPept Acc No. BAA22620) (1997) (Abstract).	
CW2		
CX2	Tada, M. et al., Database GenBank 'Online', "Homeobox protein B1X3 'Xenopus laevis'", Database Accession No. AAC61703 (29 September 1998) (Abstract)	
CY2	Tahiliani, P.D., et al., "The role of conserved amino acid motifs within the integrin $\beta_3$ cytoplasmic domain in triggering focal adhesion kinase phosphasylation". J. Biol. Chem. Vol. 272, No. 12, 7892-7898 (1997)	
CZ2	Tanaka, K., et al., "Roles of extracellular signal-regulated kinase 1/2 and p38 nitrogen- activated protein kinase in the signal transduction of basic fibroblast growth factor in endothelial cells during angiogenesis". Jpn. J. Cancer Res. 90, 647-654 (1999)	
CA3	Trikha, et al., "Role of allb83 integrin in prostate cancer metastasis", Prostate 35 (3), 185-92,	

Examiner	Date
Signature	Considered

Substitute for form 1449/PTO				Complete if Known			
				Application Number	10/575,736		
11	<b>NFORMATION</b>	1 DI	SCLOSURE	Filing Date	April 13, 2006		
S	STATEMENT BY APPLICANT			First Named Inventor	Michael V. Agrez		
				Art Unit	N/A		
(Use as many sheets as necessary)			s necessary)	Examiner Name	Not Yet Assigned		
Sheet	6	of	6	Attorney Docket Number	65350US(54086)		

	(1998).	
CB3	Townsend, P.A., et al; "\$1 integrin antisense oligodeoxynucleotides: utility in controlling osteoclast function". Eur. J. Cell. Biol. Vol.78, 485-496 (1999)	44.44
CC3	Varner, J.A. et al., "Integrin alpha 5 beta 3 expression negatively regulates cell growth: reversal by attachment to fibronectin", Mol. Biol. Cell 6, 725-740 (1995).	
CD3	Vignoud, L., et al., "NPXY motifs control the recruitment of the $a_5B_1$ integrin in focal adhesions independently of the association of talin with the $\beta_1$ chain". J. Cell. Sci. 110, 1421-1430 (1997)	
CE3	Wang, A. et al., "Differential regulation of airway epithelial integrins by growth factors", Am. J. Respira. Cell & Mol. Biol. 15, 664-672 (1996).	
CF3	Wary, K.K. et al., "The adaptor protein Shc couples a class of integrins to the control of cell cycle progression", Cell 87, 733-743 (1996).	
CG3	Weinacker et al. Role of the integrin alpha v beta 6 in cell attachment to fibronectin. J. Biol. Chem. 269:6940-6948, (1994).	
СНЗ	Yokosaki et al., "Differential Effects of the Integrins al $\beta$ , av $\beta$ , av $\beta$ 6 on Cell Proliferative Responses to Tenascin: Roles of the $\beta$ Subunit Extracellular and Cytoplasmic Domains," J. Biol. Chem., vol 271, no. 39, pp. 24144-24150, (1996).	
CI3	Yu, Y., et al., "Map Kinases, phosphatidylinositol 3-kinase, and p70 S6 kinase mediate the mitogenic response of human endothelial cells to vascular endothelial growth factor," J Cell Physiol, 178(2): 235-46, (1999).	
CJ3	Zage, P.E. and Marcantonio, E. E., "The membrane proximal region of the integrin $\beta$ cytoplasmic domain can mediate oligomerization". Cell. Adh. And Comm. Vol. 5, 335-347 (1998)	
СКЗ	Zhang, et al., "Retroviral transfer of antisense integrin $a6$ or $a8$ sequences results in laminar redistribution or clonal cell death in developing brain", J. Neurosci. 18(17), 6928-38, (1998).	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Examiner Date			
Signature Considered	Examiner	ate	 
	Signature	onsidered	

<sup>&</sup>lt;sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>Applicant is to place a check mark here if English language Translation is attached.